

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
24 August 2000 (24.08.2000)

PCT

(10) International Publication Number
WO 00/48642 A3

(51) International Patent Classification⁷: A61L 27/00,
29/00, 31/00, 33/00

(21) International Application Number: PCT/DK00/00065

(22) International Filing Date: 17 February 2000 (17.02.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 1999 00210 17 February 1999 (17.02.1999) DK

(71) Applicant (for all designated States except US): SUR-
FARC APS [DK/DK]; Hoejeloftvaenge 134, DK-3500
Vaerloese (DK).

(72) Inventors; and

(75) Inventors/Applicants (for US only): THOM, Volk-
mar [DE/US]; 164 Mill Road, Chelmsford, MA 01824
(US). JONSSON, Gunnar [DK/DK]; Hoejeloftvaenge
134, DK-3500 Vaerloese (DK). ULBRICHT, Mathias

[DE/DE]; Landsberger Allee 89, D-10407 Berlin (DE).
JANKOVA, Katja [BG/BG]; Kompl. Lazur, Todov
Kableskov Str. 12 B, 11, 8001 Burgas (BG). AL-
TANKOV, George [BG/BG]; Joliot Curie 75, bl. 313,
1113 Sofia (BG).

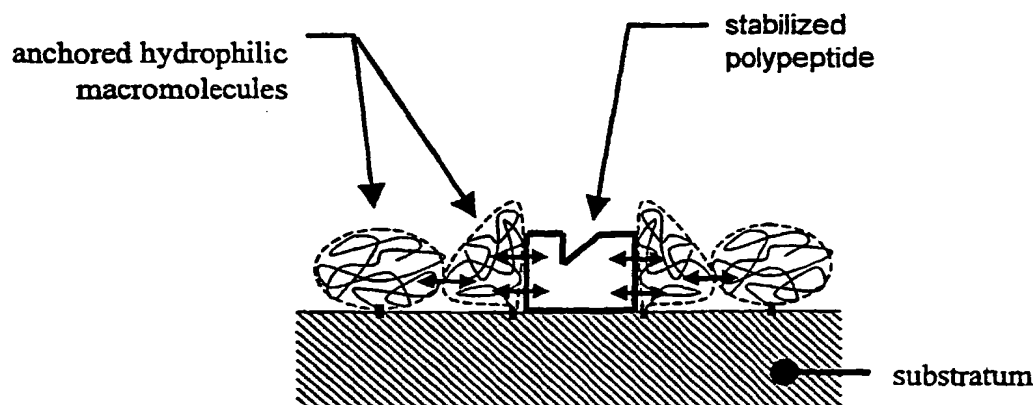
(74) Agent: HØIBERG APS; Noerre Farimagsgade 37,
DK-1364 Copenhagen K (DK).

(81) Designated States (national): AE, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK,
DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: BIOCOMPATIBLE MATERIAL WITH A NOVEL FUNCTIONALITY



(57) Abstract: The present invention is in the area of biomaterials, i.e. materials that are used in contact with living tissue and biological fluids for prosthetical, therapeutical, storage and the like. In particular, the invention relates to a novel approach of creating biocompatible surfaces, said surfaces being capable of functionally interacting with biological material. Said biocompatible surfaces comprise at least two components, such as a hydrophobic substratum and a macromolecule of hydrophilic nature, that cooperatively form a novel biocompatible surface. The novel approach is based on contacting said hydrophobic substratum with a laterally patterned monomolecular layer of hydrophilic and flexible macromolecules that exhibit a pronounced excluded volume. The surface is, in respect to polarity and morphology, a molecularly heterogeneous surface. Structural features of said macromolecular monolayer (as e.g. the layer thickness or its lateral density) are determined by, i) the structural features of the layer forming macromolecules (as e.g. their MW or their molecular architecture) and, ii) the method of creating said monomolecular layer (as e.g. by physi- or chemisorbing, or by chemically binding said macromolecules). The structural features of the layer forming macromolecule(s) is in turn determined by synthesis.



Published:

— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(88) Date of publication of the international search report:

21 December 2000

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P 405 PC00	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/DK 00/00065	International filing date (day/month/year) 17 February 2000	(Earliest) Priority Date (day/month/year) 17 February 1999
Applicant THOM, Volkmar et al.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (See Box I).
2. ☐ Unity of invention is lacking (See Box II).
3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
 - ☐ filed with the international application.
 - ☐ furnished by the applicant separately from the international application,
 - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
 - ☐ transcribed by this Authority.
4. With regard to the title, ☒ the text is approved as submitted by the applicant.
☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
 - ☒ the text is approved as submitted by the applicant.
 - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:
 - Figure No. 3 ☒ as suggested by the applicant. ☐ None of the figures.
 - ☐ because the applicant failed to suggest a figure.
 - ☐ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.
PC/PDK 00/00065**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **96-102, 105-111, 120, 122-126**
because they relate to subject matter not required to be searched by this Authority, namely:
see next page
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).:

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 00/00065

Claims 96-102, 105-111, 120, 122-126 relate to methods of treatment of the human or animal body by surgery or by therapy/diagnostic methods practised on the human or animal body/ Rule. 39.1. (iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the material.

Claim 115 can relate to a method of treatment of the human or animal body by surgery or by therapy/diagnostic methods practised on the human or animal body/ Rule. 39.1. (iv). Therefore, the search has been based on the alleged effects of the material.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 00/00065

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61L27/00 A61L29/00 A61L31/00 A61L33/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MIQIN THANG ET AL: "Proteins and cells on PEG immobilized silicon surfaces" BIOMATERIALS, vol. 19, 1998, pages 953-960, XP002928814 the whole document ---	1-146
A	DESAI N P ET AL: "Solution technique to incorporate polyethylene oxide and other watersoluble polymers into surfaces of polymeric biomaterials" BIOMATERIALS, vol. 12, March 1991 (1991-03), pages 144-153, XP002928815 the whole document --- -/--	1-146

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

19 June 2000

Date of mailing of the international search report

28 AUG 2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

E. Setréus

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DESAI N P ET AL: "Biological responses to polyethylene oxide modified polyethylene terephthalate surfaces" J. OF BIOMEDICAL MATERIALS RESEARCH, vol. 25, 1991, pages 829-843, XP002928816 the whole document ---	1-146
A	SOFIA S J ET AL: "Poly(ethylene oxide) Grafted to Silicon Surfaces: Grafting Density and Protein Adsorption" MACROMOLECULES, vol. 31, 1998, pages 5059-5070, XP002928817 the whole document ---	1-146
A	LITAUSZKI L ET AL: "Surfaces modified with PEO by the Williamson reaction and their affinity for proteins" J. OF BIOMEDICAL MATERIALS RESEARCH, vol. 35, 1997, pages 1-8, XP002928818 the whole document ---	1-146
A	WO 97 18904 A (MASSACHUSETTS INST TECHNOLOGY) 29 May 1997 (1997-05-29) page 8, line 11 -page 12, line 14; claims abstract ---	127-146
A	WO 97 46590 A (GORE ENTERPRISE HOLDINGS INC) 11 December 1997 (1997-12-11) abstract; claims; examples ---	1-146
A	WO 98 23306 A (MEADOX MEDICALS INC) 4 June 1998 (1998-06-04) abstract; claims ---	1-146
A	GING-HO HSIUE ET AL: "Platelet adhesion and cellular interaction with poly(ethylene oxide)immobilized onto silicone rubber membrane surfaces" J. BIOMATER. SCI. POLYMER EDI., vol. 7, no. 10, 1996, pages 839-855, XP002928819 the whole document ---	1-146
A	US 5 128 170 A (TANI NOBUTAKA ET AL) 7 July 1992 (1992-07-07) the whole document ---	1-146
A	US 5 512 474 A (CLAPPER DAVID L ET AL) 30 April 1996 (1996-04-30) the whole document ---	1-146
A	US 5 593 814 A (TANI NOBUTAKA ET AL) 14 January 1997 (1997-01-14) the whole document ---	1-146
	--- -/--	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PARK A ET AL: "Integration of surface modification and 3D fabrication techniques to prepare patterned poly(L-lactide) substrates allowing regionally selective cell adhesion"</p> <p>J. BIOMATER. SCI. POLYMER EDN., vol. 9, no. 2, 1998, pages 89-110, XP002114420 the whole document</p> <p>---</p>	1-146
A	<p>WO 98 47948 A (CALIFORNIA INST OF TECHN) 29 October 1998 (1998-10-29) the whole document</p> <p>---</p>	1-146
A	<p>ROBERTS C ET AL: "Using Mixed Self-Assembled Monolayers Presenting RGD and (EG)30H Groups To Characterize Long-Term Attachment of Bovine Capillary Endothelial Cells to Surfaces"</p> <p>J. AM. CHEM. SOC., vol. 120, 1998, pages 6548-6555, XP002928821 abstract Results</p> <p>---</p>	1-146
A	<p>US 5 330 911 A (HUBBELL JEFFREY A ET AL) 19 July 1994 (1994-07-19) abstract; claims</p> <p>-----</p>	1-146

INTERNATIONAL SEARCH REPORT
 Information on patent family members

02/12/99

International application No.

PCT/DK 00/00065

Patent document cited in search report			Publication date	Patent family member(s)		Publication date
WO	9718904	A1	29/05/97	NONE		
WO	9746590	A1	11/12/97	AU	3229797 A	05/01/98
				EP	0910584 A	28/04/99
				US	5874165 A	23/02/99
				US	5897955 A	27/04/99
				US	5914182 A	22/06/99
WO	9823306	A1	04/06/98	AU	5263398 A	22/06/98
				EP	0946217 A	06/10/99
				US	5877263 A	02/03/99
US	5128170	A	07/07/92	DE	69018691 D,T	17/08/95
				EP	0397130 A,B	14/11/90
				JP	2620378 B	11/06/97
				JP	3103264 A	30/04/91
				JP	9103481 A	22/04/97
				US	5240747 A	31/08/93
US	5512474	A	30/04/96	NONE		
US	5593814	A	14/01/97	DE	69013764 D,T	30/03/95
				EP	0402718 A,B	19/12/90
				JP	2023897 C	26/02/96
				JP	3007576 A	14/01/91
				JP	7051061 B	05/06/95
				US	5202227 A	13/04/93
				JP	3007577 A	14/01/91
WO	9847948	A1	29/10/98	AU	7121198 A	13/11/98
US	5330911	A	19/07/94	AT	153064 T	15/05/97
				AU	646644 B	03/03/94
				AU	6447290 A	28/04/91
				CA	2066213 A	29/03/91
				DE	69030730 D,T	02/01/98
				DK	494216 T	24/11/97
				EP	0494216 A,B	15/07/92
				ES	2102366 T	01/08/97
				JP	5502998 T	27/05/93
				US	5278063 A	11/01/94
				WO	9105036 A	18/04/91